Remarks

Reconsideration is respectfully requested in light of the foregoing amendment and the remarks that follow.

Claims 36-37, 39-43, 45-52 and 54-56 are pending in this application. Claims 57-59 have been cancelled. Claims 36, 42 and 48 have been amended to include the subject matter of the cancelled claims.

Claims 36-40, 42-46, and 48-54 are rejected under 35 U.S.C. § 103(a) as obvious over Ukai et al. (U.S. Patent No. 6,576,677).

Applicant respectfully submits that the obviousness rejection must be viewed in terms of the claim language and the actual teachings present in Ukai. To this end, the independent claims now recite polyvinylpyrrolidone having an average molecular weight from about 10,000 to about 40,000. (This should permit a more meaningful comparison between the data and examples of the instant specification and those of the reference. The molecular weights are the same.)

It should also be noted that the claims require a basic or neutral pH which is distinct from the acidic range taught by Ukai et al. See col. 3 at lines 8-9. Further, the instant specification teaches the use of polyvinylpyrrolidone as suspending agents. See line 10 on page 29. This function is distinct from the making effect taught by Ukai et al. for polyvinylpyrrolidones The polyvinylpyrrolidone amounts which achieve these distinct functions are distinct- 250 mg/5 ml for the masking effect (Ukai et al Tables 4 and 5) v 50 mg/5ml for the suspending function taught (Applicants' Table (p.31)).

Ukai et al. teach basic medicaments have an unpleasant taste.[1] Further, Ukai et al. teach that this taste can be remedied by the presence of polyvinylpyrrolidones in sufficient amounts so that two pyrolidone groups trap the positively charged proton and thereby block the contact of the basic medicament with a taste bud. At column 5, lines 1-7, Ukai teaches that the masking effects are heightened with increased amounts of polyvinylpyrrolidone. See Table 2. At column

[1] The basic medicaments at issue are those in which a proton exists as a positive charge under acidic conditions, e.g. Donepezil hydrochloride.

2, lines 60-62, Ukai teaches that the "larger the molecular weight of polyvinylpyrrolidone, the less the amount of it to be added, while the smaller, the more the amount to be added." The present claims permit a cleaner comparison of the claims with the amounts taught by the reference without concerns relative to the impact of comparing a lesser amount of a higher molecular weight polyvinylpyrrolidone.

The Examiner's position appears to be that optimization of the Ukai amounts would meet those required by the claims. It is respectfully submitted that as to the amended claims optimization as to the masking effect taught by Ukai et al. would lead to increased amounts of polyvinylpyrrolidone rather than the lower amounts required by the claims. Compare Tables 4 and 5 (250 mg) with the instant Table on page 31 (50mg). There is a five fold difference in amounts. The amount required for the Ukai et al. masking effect- 250mg- is far greater than that required for Applicants' suspending effect- 50 mg.

The Examiner's reasoning in the Office Action does not apply to claims where the formulation comprises polyvinylpyrrolidone having an average molecular weight the same as or lower than the average molecular weight of polyvinylpyrrolidone described and exemplified in Ukai (i.e., polyvinylpyrrolidone having an average molecular weight of 40,000). With respect to polyvinylpyrrolidones having a lower average molecular weight, Ukai teaches that a larger amount (i.e., > 2%) of such low molecular weight polyvinylpyrrolidone would be required in order to reduce the bitter taste and numbing qualities of the formulation to an acceptable level. Applicant respectfully submits that a person of skill in the art of pharmaceutical formulations would consider optimization based on Ukai to lead one to larger amounts of polyvinylpyrrolidone, not lesser amounts.

Further, the solubility of the donepezil hydrochloride decreases as the pH becomes neutral and alkaline. The solubility is as follows: at a pH of 5.83, it is 12.16 mg/ml; at a pH of 8.40, it is 0.0098 mg/ml. The pH range set forth in claims 36, 42 and 48 is from 6.5 to 9. In claims 39, 45 and 54, the pH range is from 7 to 8.5. The drug state in Example 1 and within the claimed ranges would be a suspension and not as a solution. In a solution state like that of Ukai et al. (acidic pH), the bitter taste is masked by binding the drug to render it sterically hindered

and not accessible to the taste buds. At an alkaline or neutral pH, the drug is not in solution and presumably not accessible to the taste bud as taught by Ukai et al. The bitter taste due to donepezil hydrochloride would not be expected to be present at neutral and alkaline pH since donepezil hydrochloride would not be in solution. The need for masking using polyvinylpyrrolidone would not be apparent.

Applicant respectfully requests that the rejection under 35 U.S.C. § 103 be withdrawn since a proper prima facie case has not been established.

Claims 41, 47, and 55 are rejected under 35 U.S.C. § 103(a) as obvious over Ukai et al. as applied to claims 36, 37, 39-40, 42, 43, 45-46, 48-52, 54 and 56-59 above, and further in view of Sugimoto et al., U.S. Patent No. 4,895,841.

The deficiencies noted above for Ukai et al. are not remedied by the teaching provided by Sugimoto et al.

Accordingly, withdrawal of the rejection is respectfully requested for the reasons given above.

Conclusion

An early and favorable reconsideration and allowance of pending claims 36-37, 39-43, 45-52 and 54-56 is respectfully requested.

Respectfully submitted,

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